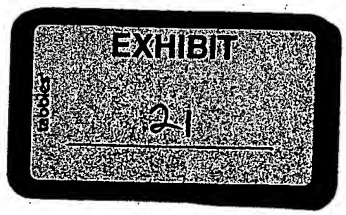

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Apoptosis-related proteins, BCL-2, BAX, FAS, FAS-L and PCNA in liver biopsies of patients with chronic hepatitis B virus infection.

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While the elimination of hepatitis B virus (HBV) is a common phenomenon at the end of the acute phase of disease, the persistence of HBV is characteristic for chronic hepatitis (CHB). Recent evidence indicates that the elimination of HBV is achieved by FAS/FAS-L induced apoptosis of infected hepatocytes. The aim of this study was to test the hypothesis that HBV persistence in the hepatocytes of CHB patients is due to the delayed onset of apoptosis caused by altered FAS/FAS-L interactions between lymphocytes and hepatocytes. The expression of FAS, FAS-L, BAX, BCL-2, ICE and PCNA in the liver biopsies of 55 patients (14 HBsAg positive, 20 patients with alcoholic hepatopathy, 21 patients with other hepatopathies) was tested by immunohistochemistry. Apoptosis of hepatocytes was evaluated by morphological as well as by TUNEL method. The results were correlated with a grading/staging score and analysed statistically using a one way analysis of variance and the Duncan test. Significantly highernumbers of BAX positive hepatocytes were observed in HBsAg positive patients when compared to control groups. Similarly, both BAX and FAS positive lymphocytes were more frequent in HBsAg positive patients. FAS-L positive lymphocytes and hepatocytes were numerous in all patient groups. Increased numbers of BAX positive hepatocytes in CHB may reflect the increased readiness of these cells to undergo apoptosis. However, the increased numbers of both BAX and FAS positive lymphocytes in CHB suggest that these cells may be particularly sensitive to FAS-L mediated apoptosis potentially resulting in lowered viability of these lymphocytes. This may explain, at least in part, the defective removal of virus-infected cells in chronic hepatitis. However, we cannot rule out the possibility that survival of hepatocytes during CHB may be due to other mechanisms such as defects in apoptosis activation triggered by CD40, defects involving DNase and/or other caspases downstream in the apoptotic cascade within these cells, or to defects in CTL function.